

APPLICATION  
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TITLE: COMPOSITION FOR ENHANCING PHYSICAL  
PERFORMANCE

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# COMPOSITION FOR ENHANCING PHYSICAL PERFORMANCE

## **CROSS REFERENCE TO RELATED APPLICATION**

This application is a continuation-in-part of U.S. Application Serial No.10/302,544, filed November 22, 2002. This application also claims priority to U.S. Application Serial No. 60/420,986, filed October 23, 2002.

## **BACKGROUND**

Achieving peak physical performance has long been a goal for athletic competition and self-improvement. Means for improving physical performance includes prolonged systematic exercise, proper diet, and use of pharmaceuticals such as anabolic steroids. Anabolic steroids, which are testosterone derivatives, promote tissue growth, increase muscle mass, increase blood volume and hemoglobin level, and improve overall strength. Nonetheless, the use of anabolic steroids often results in serious complications, such as decreased blood high-density lipoprotein levels, disorders of the reproductive system, and disorders of the liver including carcinoma and peliosis hepatis. These complications further lead to virilization in females, interrupted growth in children, and defects in fetuses. The use of anabolic steroid can also cause psychological disorders such as unpredictable mood changes and aggression. Thus, there is a need for a safe drug or dietary supplement for enhancing physical performance.

## **SUMMARY**

This invention relates to a composition that contains quercetin and a number of other natural products. The composition can be used in enhancing physical performance, i.e., improving an ability to perform an exercise, such as speed, strength, power, endurance, flexibility, agility, balance, focus coordination, reaction time, and fatigue recovery.

One aspect of this invention features a composition that contains quercetin and one or both of vitamin B3 and vitamin C. In one embodiment, the composition further contains at least one of the following ingredients: vitamin B1, vitamin B2, vitamin B6, and vitamin B12. In another embodiment, it further contains at least one of caffeine, epigallocatechin gallate, epicatechin, epicatechin gallate, epigallocatechin, and polyphenon E. This composition may also contain other ingredients, such as vitamin E, CoQ-10, soy isoflavones, taurine, sugar beet pectin

fiber, and a ginko biloba extract. Further, the composition can be sweetened, if necessary, by adding a sweetener, e.g., sorbitol, maltitol, cane sugar, high fructose corn syrup, and the like. The composition can also contain amino acids, minerals, a flavor enhancer, or a coloring agent. It is known that the leaves of green tea contain epigallocatechin gallate, epicatechin, epicatechin gallate, epigallocatechin, and polyphenon E. Thus, these five ingredients can be conveniently provided as a green tea extract.

The composition of the invention can be in dry form (e.g., powder or tablet) or in aqueous form (e.g., beverage or syrup). It can be a dietary supplement or a pharmaceutical formulation. It can also be a drink or a food product. Examples include tea (e.g., a tea drink and the contents of a tea bag), soft drinks, juice (e.g., a fruit extract and a juice drink), milk, coffee, jelly, ice cream, yogurt, cookies, cereals, chocolates, and snack bars. The composition, in any of the forms described above, can be used to enhance physical performance. Also within the scope of this invention is a composition of the invention as an active agent, as well as use of the composition for the manufacture of a medicament, for enhancing physical performance.

The invention also features a method for enhancing physical performance. The method includes administering to a subject in need thereof an effective amount of the above-described composition. By proper administering the composition as detailed below, physical performance can be enhanced without the deleterious side effects of pharmaceutical performance enhancers, such as anabolic steroids.

The details of one or more embodiments of the invention are set forth in the accompanying description below. Other features, objects, and advantages of the invention will be apparent from the description and from the claims.

## DETAILED DESCRIPTION

This invention is based, at least in part, on the unexpected discovery that quercetin, an antioxidant, and a number of other natural products exhibit synergistic health benefits, including enhancing physical performance in a subject.

For example, within the scope of this invention is a quercetin-containing composition that includes vitamin B3 or vitamin C, or both. It further contains one or more of vitamin B1, vitamin B2, vitamin B6, and vitamin B12. The composition can also contain one or more of caffeine, epigallocatechin gallate, epicatechin, epicatechin gallate, epigallocatechin, and

polyphenon E. A green tea extract can be conveniently used to provide epigallocatechin gallate, epicatechin, epicatechin gallate, epigallocatechin, and polyphenon E.

Exemplary quantities of the ingredients of this composition are: 0.1-50 mg of vitamin B1, 0.1-150 mg of vitamin B2, 0.1-2000 mg of vitamin B3, 0.1-200 mg of vitamin B6, 5-150 µg of vitamin B12, 50-2000 mg of vitamin C, 50-1500 mg of caffeine, 20-2000 mg of quercetin, 10-500 mg of epigallocatechin gallate, 10-500 mg of epicatechin, 10-500 mg of epicatechin gallate, 10-500 mg of epigallocatechin, and 10-500 mg of polyphenon E, which can be dissolved or dispersed in a 1 L aqueous solution. The quantities of the ingredients can also be those of the same relative ratio to those listed above. The term "quercetin" refers to both quercetin aglycon and quercetin derivatives, e.g., quercetin-3-O-glucoside, quercetin-5-O-glucoside, quercetin-7-O-glucoside, quercetin-9-O-glucoside, quercetin-3-O-rutinoside, quercetin-3-O-[α-rhamnosyl-(1→2)-α-rhamnosyl-(1→6)]-β-glucoside, quercetin-3-O-galactoside, quercetin-7-O-galactoside, quercetin-3-O-rhamnoside, and quercetin-7-O-galactoside. After digestion, quercetin derivatives are converted to quercetin aglycon, an active form absorbed in the body. The quantity of quercetin mentioned above refers to that of quercetin aglycon or the quercetin moiety of a quercetin derivative. As an example, a composition for daily use can be a 1 L aqueous solution containing 1000 mg of quercetin, 30 mg of vitamin B1, 85 mg of vitamin B2, 1 g of vitamin B3, 100 mg of vitamin B6, 120 µg of vitamin B12, 1200 mg of vitamin C, 1000 IU of vitamin E, 1000 mg of caffeine, and a green tea extract containing 120 mg of epigallocatechin gallate, 140 mg of epicatechin, 360 mg of epicatechin gallate, 360 mg of epigallocatechin, and 120 mg of polyphenon E.

This composition may also contain one or more other active ingredients, such as vitamin E, CoQ-10, soy isoflavones, taurine, sugar beet pectin fiber, and a ginkgo biloba extract. Exemplary quantities of these ingredients are: 3-1000 IU of vitamin E, 10-400 mg of CoQ-10, 20-600 mg of soy isoflavones, 10-1000 mg of taurine, 1-15 g of sugar beet pectin fiber, and 50-500 mg of a ginkgo biloba extract (dry weight). Further, the composition can be sweetened, if necessary, by adding a sweetener such as sorbitol, maltitol, hydrogenated glucose syrup and hydrogenated starch hydrolyzate, high fructose corn syrup, cane sugar, beet sugar, pectin, and sucralose.

An example of the above-described composition is a powder. It can be used conveniently to prepare beverages, e.g., tea or juice. The powder can also be used to prepare paste, jelly,

capsules, or tablets. Lactose and corn starch are commonly used as diluents for capsules and as carriers for tablets. Lubricating agents, such as magnesium stearate, are typically added to form tablets.

The composition of this invention can also be a dietary supplement or a pharmaceutical formulation. As a dietary supplement, additional nutrients, such as minerals or amino acids may be included. The composition can also be a drink or food product. As used herein, the terms “drink” and “food” broadly refer to any kinds of liquid and solid/semi-solid materials, respectively, that are used for nourishing an animal, and for sustaining normal or accelerated growth of an animal including a human. Examples of the drink product include, but are not limited to, tea-based beverages, juice, coffee, and milk. Examples of the food product include jelly, cookies, cereals, chocolates, snack bars, herbal extracts, dairy products (e.g., ice cream, and yogurt), soy bean product (e.g., tofu), and rice products.

The above-described composition, in any of the forms described above, can be used for enhancing physical performance. As shown in the examples below, the composition improves overall strength, balance, fatigue recovery, intensity of physical exercise, and endurance to the exercise. It can also be used for treating diseases or disorders, such as arthritis, tumor, diabetes, sexual dysfunction, chronic constipation, inflammatory bowel disease; improving concentration or mood; and lowering cholesterol levels or blood pressure. A “tumor” refers to benign tumor, as well as malignant tumor (e.g., leukemia, colon cancer, kidney cancer, liver cancer, breast cancer, or lung cancer).

The terms “improving”, “treating,” and “lowering” refer to the administration of an effective amount of a composition of the invention to a subject, who needs to improve his physical performance or has one or more of the just-mentioned disorders, or a symptom or a predisposition of one of more of the disorders, with the purpose to improve physical performance or to cure, alleviate, relieve, remedy, or ameliorate one or more of the disorders, or the symptoms or the predispositions of one or more of them. The term “administration” covers oral or parenteral delivery to a subject a composition of the invention in any suitable form, e.g., food product, beverage, tablet, capsule, suspension, and solution. The term “parenteral” refers to subcutaneous, intracutaneous, intravenous, intramuscular, intraarticular, intraarterial, intrasynovial, intrasternal, intrathecal, intralesional, and intracranial injection, as well as various infusion techniques. An “effective amount” refers to a dose of the composition that is sufficient

to provide a physical benefit (e.g., improving endurance) or a therapeutic benefit (e.g., lowering cholesterol levels or blood pressure). Both *in vivo* and *in vitro* studies can be conducted to determine optimal administration routes and doses.

The specific examples below are to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever. Without further elaboration, it is believed that one skilled in the art can, based on the description herein, utilize the present invention to its fullest extent. All publications cited herein are hereby incorporated by reference in their entirety.

#### Example 1

Composition A (1000 ml) was prepared by mixing the following ingredients at room temperature: 1000 ml of orange juice, 1000 mg of quercetin, 30 mg of vitamin B1, 85 mg of vitamin B2, 1000 mg of vitamin B3, 100 mg of vitamin B6, 120 µg of vitamin B12, 1000 IU of vitamin E, and 1000 mg of caffeine. All ingredients were obtained from Spectrum Laboratory Products, Inc., Gardena, CA; Sigma, St. Louis, MO; and Aldrich, Milwaukee, WI.

Ten male Sprague-Dawley rats, weighing 240-250 g, were obtained from Charles River Lab (Boston, MA). The rats were divided into Groups 1 and 2 (5 in each group). The rats in the Group 2 were administered by intragastric feeding with the just-described composition at a daily dose of 8 ml/rat (30 ml/kg body weight) for 48 days. The rats in Group 1 were administered with water.

At days 0, 14, 28, and 42 after the administration, blood samples were collected from the rats by supraorbital bleeding and various hematological parameters were determined using standard methods. The results are summarized in Tables 1 and 2 below.

**Table 1. Effects of composition A on rat hematological parameters**

Parameter	Reference Range	Day 0		Day14		Day 28		Day 42	
		Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
WBC	9.4-14.9 (THSN/UL)	17.22	15.04	17.34	16.50	18.76	16.90	17.66	14.20
RBC	6.2-9.0 (MILL/UL)	6.09	5.94	6.63	6.60	7.43	7.20	7.99	7.72
Hb	13.4-16.4 (GM/DL)	12.46	12.38	14.24	14.40	15.32	15.02	15.86	15.18
Hematocrit	40.0-49.0 (%)	37.80	37.44	42.30	43.26	45.56	45.00	47.04	45.86
MCV	52.0-66.0 (FL)	62.20	63.20	63.80	65.40	61.60	62.60	58.80	59.40
MCH	17.7-19.1 (PICO GM)	20.46	20.84	21.50	21.82	20.68	20.86	19.88	19.72
MCHC	32.0-33.5 (%)	32.96	33.00	33.64	33.26	33.66	33.38	33.72	33.14
Platelet	780-1400 (THSN/UL)	956.00	965.00	1084.60	1158.80	1078.40	1076.60	967.00	962.80
BANDS	0.00-0.06 (THSN/UL)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Segmented Neutrophiles	0.58-6.30 (THSN/UL)	4.44	4.78	3.34	3.59	3.41	3.33	3.27	3.60
Lymphocyte	3.78-14.9 (THSN/UL)	10.07	7.84	12.10	11.02	13.52	11.99	12.78	9.37
Monocyte	0.02-1.20 (THSN/UL)	3.43	2.15	1.67	1.67	1.49	1.30	1.24	1.03
Eosinophiles	0.00-0.01 (THSN/UL)	0.54	0.16	0.11	0.10	0.17	0.13	0.20	0.10
Basophiles	0.00-0.00 (THSN/UL)	0.14	0.11	0.12	0.12	0.17	0.15	0.16	0.09
Atipicle Lymphocyte	0.00-0.00 (THSN/UL)	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Metamyelocytes	0.00-0.00 (THSN/UL)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Myelocytes	0.00-0.00 (THSN/UL)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
NRBC/100WBC	0-0 (/100WBC)	0.60	0.40	0.00	0.00	0.00	0.00	0.00	0.00
Reticulocyte	0.1-4.0 (%)	1	1	2.62	5.74	3.30	5.90	4.78	6.58

Note:

WBC: white blood cell

RBC: red blood cell

Hb: hemoglobin

MCV: mean corpuscular volume

MCH: hemoglobin amount per red blood cell

MCHC: mean cell hemoglobin concentration

BANDS: premature neutrophil

NRBC: nucleated red blood cell count

THSN/UL: 1,000/ul

MILL/UL: 1,000,000/ul

GM/DL: gram/dl

FL: femtoliter

PICO GM: picogram

**Table 2. Effects of composition A on rat reticulocyte level**

Group	Ref. Range (%)	Day	Reticulocyte level in each rat					Average	SD
			1#	2#	3#	4#	5#		
1	0.1-4.0	14	2.9	2.9	2	4.9	4.4	2.62	0.96
2	0.1-4.0	14	5.8	4.9	7.5	5.8	4.7	5.74	2.15
1	0.1-4.0	28	3.1	2.2	2.2	7.2	6.8	3.30	2.5
2	0.1-4.0	28	4.8	6.5	5.4	5.5	7.3	5.90	1.3
1	0.1-4.0	42	4.8	9.2	9	5.5	5.4	4.78	2.14
2	0.1-4.0	42	7.5	6.2	6.1	6.4	6.7	6.58	0.16

Note: SD = Standard Deviation

As shown in Tables 1 and 2, the reticulocyte levels in the rats administered with composition B (Group 2) were higher than those in the rats administered with water (Group 1). For example, at Day 42, the average reticulocyte level in the rats of Group 2 (6.58%) was higher than that in the rats of Group 1 (4.78%) by 37.7%. On the other hand, other hematological parameters of the rats in the two groups did not differ significantly. See Table 1. These results indicate that composition A increases the reticulocyte level but does not affect other hematological parameters. Reticulocytes are immature, anucleated red blood cells (RBCs). An increase in the reticulocyte level and no changes in other hematological parameters suggest that composition A improves the renewal of RBC.

During the experiment, the body weight of each rat was monitored daily. No statistical difference was found between the two groups.

### Example 2

Composition B (1000 ml) was prepared by mixing the following ingredients at room temperature: 1000 ml of orange juice, 1000 mg of quercetin, 30 mg of vitamin B1, 85 mg of vitamin B2, 1000 mg of vitamin B3, 100 mg of vitamin B6, 120 µg of vitamin B12, 1000 IU of vitamin E, 1000 mg of caffeine, 500 mg of epigallocatechin gallate, 500 mg of epicatechin, 500 mg of epicatechin gallate, 500 mg of epigallocatechin, and 500 mg of polyphenon E.

Ten male Sprague-Dawley rats that weighed 240-250 g were divided into Groups 1 and 2 (5 in each group). The rats in Group 2 were administered by intragastric feeding with composition B at an average daily dose of 14 ml/kg body weight for 95 days. Those in Group 1 were administered with water.

Starting from Day 92 after the administration, each of the rats was trained on a Rota-Rod treadmill (Model 57750, Stoelting Co., Wood Dale, Illinois) for over 2 hours. At Day 95, after



being trained for another 20 minutes, each of the rats was put on the treadmill and allowed to walk. The time for which each rat walked on the treadmill before falling off was recorded and the average time for the rats in Groups 1 and 2 determined. The experiments were repeated for three times ("Test A," "Test B," and "Test C"). The results are summarized in Table 3 below.

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**Table 3. Effects of composition B**

Groups	Time on Rota-Rod treadmill (min)		
Group 1	Test A	Test B	Test C
#1	2.36	13.11	23.33
#2	10.69	16.02	44.21
#3	19.02	15.46	66.90
#4	2.99	16.67	16.09
#5	1.34	3.41	7.82
Average	<b>7.28</b>	<b>12.93</b>	<b>31.67</b>
SE	3.37	2.45	10.68
Group 2			
#1	6.54	61.95	80.40
#2	16.16	21.54	41.73
#3	6.91	23.83	90.47
#4	24.19	20.42	202.82
#5	32.58	15.37	67.44
Average	<b>17.28</b>	<b>28.62</b>	<b>96.57</b>
SE	5.03	8.45	27.79

Note: SE = Standard Error

As shown in Table 3, the rats got used to the exercise and walked for longer time on the treadmill as the experiment went on. In all tests, the rats that had been administered with composition B walked on the treadmill longer than those that had been not. These results indicate that composition B enhanced the physical performance of rats. During the 95 days of administration, the body weight of each rat was monitored daily. No statistical difference was found between Groups 1 and 2. This result suggests the enhanced physical performance of the rats in Group 2 was not due to an increase in body mass.

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## OTHER EMBODIMENTS

All of the features disclosed in this specification may be combined in any combination. Each feature disclosed in this specification may be replaced by an alternative feature serving the same, equivalent, or similar purpose. Thus, unless expressly stated otherwise, each feature disclosed is only an example of a generic series of equivalent or similar features.

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From the above description, one skilled in the art can easily ascertain the essential characteristics of the present invention, and without departing from the spirit and scope thereof, can make various changes and modifications of the invention to adapt it to various usages and conditions. Thus, other embodiments are also within the scope of the following claims.